

**REMARKS**

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 1-8, 10-36, 38-41 and 43-44 are in this Application. Claims 24, 25 and 35-39 have been withdrawn from consideration. Claims 1-23, 26-34 and 40-44 have been rejected. Claims 9, 37 and 42 have been canceled. Claims 1, 10, 14, 26, 29, 35, 36, 38 and 43 have been amended. New claims 45-47 have been added.

**35 U.S.C. § 101 Rejection**

The Examiner rejects claims 1 and 26 under 35 U.S.C. § 101 as being directed to non-statutory subject matter. The Examiner states that the claims analyze data of a reordered distance matrix, but do not require the use of a computer or other device.

Without acquiescing to the propriety of the § 101 rejection, and in a good-faith attempt to further prosecution, Applicant has amended independent claims 1 and 26 to include use of computer and display of the structure of the data.

In light of this amendment, Applicant respectfully requests withdrawal of the rejection.

**35 U.S.C. § 112 Rejection**

Claim 42 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 42 canceled thereby rendering moot the Examiner rejection with respect thereto.

**35 U.S.C. § 103 Rejection - Skierczynski et al. in view of Roberts**

Claims 1-8, 20-22, 40, 42 and 44 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Skierczynski et al. in view of Roberts.

The Examiner states that Skierczynski et al. shows analysis of data by use of an ordered distance matrix, a non-hierarchical clustering and generation of a hierarchical tree to show results. The Examiner acknowledges that Skierczynski et al. does not show reordering a previously ordered distance matrix, or explicitly using an unsupervised analysis, but nevertheless states that Roberts shows that hierarchical

supervised clustering produces a dendrogram tree result, and that unsupervised clustering is an alternative clustering method that does not have an a priori number of partitions. The Examiner concludes that it would have been obvious to a person of ordinary skill in the art at the time the invention was made to reorder a distance matrix because Skierczynski et al. show ordering is applied to a distance matrix, and therefore Skierczynski et al. applies a new order to a previously unordered distance matrix.

The Examiner further states that Roberts shows that hierarchical clustering is known as supervised and non-hierarchical clustering is known as unsupervised, and concludes that Skierczynski et al. shows alternatives of using either supervised or unsupervised clustering methods because they show use of either hierarchical or non-hierarchical clustering methods.

The Examiner's rejection is respectfully traversed. Roberts does not provide what Skierczynski et al. lack.

Applicants respectfully disagree with the Examiner that Roberts shows that hierarchical clustering is supervised and non-hierarchical clustering is unsupervised. Roberts describes various clustering techniques which he refers to as "unsupervised." However, nowhere in Roberts is there any reference to supervised clustering or non-hierarchical clustering or the differences therebetween. In this respect, the Examiner's interpretation of Roberts appears to be incorrect. It is therefore submitted that the combination suggested by the Examiner would not produce the claimed subject matter.

Skierczynski et al. disclose a clustering technique which includes a hierarchical clustering algorithm combined with a non-hierarchical clustering. The hierarchical clustering is used for determining the optimal number of clusters and the non-hierarchical clustering is used for distributing the members of the sample into the optimal number of clusters. Skierczynski et al. also disclose constructing a distance matrix that includes distance data (Column 18 lines 38-52). However, as properly noted by the Examiner, Skierczynski et al do not teach reordering of the data.

Applicants disagree with the Examiner's statements that Skierczynski et al. apply a new order to a previously unordered distance matrix. Skierczynski et al. do not even hint at applying order to the distance matrix. It is correct that the term "ordered set" appears many times throughout Skierczynski's discloser, but the action

of reordering the distance matrix is not disclosed, explicitly or implicitly. Nevertheless, in order to expedite prosecution of this case, Applicants have introduced into claim 1 the feature of performing at least one permutation of the objects to provide a reordered distance matrix describing distances between objects in the reordered set. This feature finds support throughout the specification, see, *e.g.*, Paragraphs 3 and 23 of the published application (U.S. Published Application No. 2007/0288540). It is noted that the amendment to claim 1 does not make the claim narrower. In particular, the deletion of the word "unsupervised" broadened the claim.

It is submitted that claim 1 is not rendered obvious since neither Skierczynski nor Roberts teaches reordering of the distance matrix, and certainly not performing permutation of the objects to provide a reordered distance matrix and analyzing the reordered distance matrix so as to determine the structure of the data featured by the reordered distance matrix.

Claims 2-8, 20-22, 42, 44 and 46 all depend from claim 1 and are therefore submitted to be allowable together with that claim, apart from the further features set forth in the respective claims. It is to be noted, however, that many of these claims set forth even further distinguishing features.

For example, claim 10 includes the distinguishing feature that the permutation comprises the Side-to-Side method and claim 14 includes the distinguishing feature that the permutation comprises the Neighborhood method. These methods are neither disclosed nor implied by Skierczynski et al. and/or by Roberts.

Claim 44 includes the distinguishing feature that the reordering is constrained according to a dendrogram from hierarchical clustering method. It is noted that this feature differs from Skierczynski et al., since Skierczynski does not use the hierarchical clustering for constraining the reordering. Rather, Skierczynski applies the hierarchical clustering to the distance matrix in order to produce a dendrogram (see, for example, Column 18 lines 53-65).

Claim 46 includes the distinguishing feature that the permutation of the objects to provide the reordered distance matrix comprises searching for a minimum of an energy function. Support for this feature is found throughout the specification, see, for example, Paragraphs 39, 44 and 55 of the published application. Skierczynski does not teach or imply searching for any minimum, nor does he teach permutation of the objects which comprises searching for a minimum an energy function.

**35 U.S.C. § 103 Rejection - Skierczynski et al. in view of Roberts and Golub et al**

The Examiner rejects claims 1, 23, 26, 30 and 31 under 35 U.S.C. §103(a) as being unpatentable over Skierczynski et al. in view of Roberts as applied to claims 1-8, 20-22, 40, 42 and 44, and further in view of Golub et al. The Examiner acknowledges that Skierczynski et al. in view of Roberts do not show data of cancerous tissue or filtering of data and analysis of noise level. The Examiner states that Golub et al. shows analysis of gene expression data, and that the clustering analysis allows for ALL and AML to be distinguished by gene expression analysis. The Examiner further states that Golub et al. shows quality control analysis of samples and exclusion of data if there is a low signal or aberrant signal images. The Examiner holds that it would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Skierczynski et al. in view of Roberts by filtering aberrant data because Golub et al. shows that expression analysis of microarrays should have data removed if the signals are low or aberrant. The Examiner also holds that it would have been further obvious to analyze samples of cancerous tissue because Golub et al. shows clustering analysis of leukemia cells is useful to distinguish between AML and ALL.

The Examiner's rejection are respectfully traversed. Golub does not provide what Skierczynski et al. and Roberts lack.

The following relates to independent claims 1 and 26, the dependent claims are submitted to be patentable at least by virtue of their dependency on the parent claims.

Golub et al. discloses a systematic approach to cancer classification based on the simultaneous expression monitoring of genes using DNA microarrays. To cluster tumors, Golub used self-organizing maps, in which the number of clusters to be identified is specified by the user (see page 533 right column third paragraph). Golub is completely silent with respect to reordering of a distance matrix, and certainly with respect to permutation of the objects in the distance matrix to provide a reordered distance matrix.

It is therefore submitted that claims 1 and 26 are not rendered obvious since none of Skierczynski, Roberts and Golub teach performing permutation of the objects

to provide a reordered distance matrix and analyzing the reordered distance matrix so as to determine the structure of the data featured by the reordered distance matrix.

**Examination of Generic and Non-Elected Claims**

In view of the amendments made to the claims and the arguments recited herein it is believed that the claims are allowable with respect to the elected species and hence examination of claims 1 in its generic context and with respect to all the species recited therein, as well as examination of claims 24, 25, 35, 36, 38 and 39 is respectfully requested.

In view of the above amendments and remarks it is respectfully submitted that the claims are now in condition for allowance. A prompt notice of allowance is respectfully and earnestly solicited.

Respectfully submitted,

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**Enclosures:**

- Petition for Extension (One Month)
- Additional Claims Transmittal Fee